influenced, although the patients died. Much depends upon technique, the proper dosage, and intervals of dosage, as well as upon bringing the patient promptly under treatment before destructive lesions have developed in organs other than the heart. The difficulty of not always obtaining a positive blood culture from which to prepare an homologous vaccine may be overcome sometimes in other ways. In one of the cases of this series vaccines were made from streptococci derived from the patient's septic uterus, and subsequently from an abscess in the arm. In another case the vaccine was derived from pus in the knee-joint. The cultures and vaccines employed in the described cases were prepared for me by Prof. T. W. Hastings, of the Cornell University Medical School, and Dr. J. C. Meakins, of the pathological department of the Presbyterian Hospital, the vaccines being derived in each case strictly in accordance with the method originally devised by Wright.

As the subject is a new and important one, I have reported the fatal as well as the cured cases, with some degree of detail, for in several of the fatal cases the vaccines produced marked temporary beneficial effect, and the patient apparently was cured of sepsis, only to die of some other disease. In summary: Of the seven cases of septic endocarditis, three were cured by homologous vaccines; in two fatal cases the effect upon the septic phenomena was striking and temporarily beneficial, and in two fatal cases it was slight, but clearly demonstrable. In addition, one advanced case of pyemia was cured.

ACUTE GANGRENOUS PANCREATITIS.

By Louis Jurist, M.D.,
of Philadelphia.

The number of cases of gangrenous pancreatitis, especially of those eventuating in recovery, that have been reported, is so small that an additional case may be of value in bringing forward diagnostic and therapeutic points.

H. M. N., a male, aged thirty-nine years, a merchant, is an only child. His father died of some liver condition associated with ascites. His mother is living, but is a diabetic. The patient has had the ordinary diseases of childhood, typhoid fever when a boy, and pneumonia at the age of twenty-five years. He is married and has two children. living and well. He is temperate, fond of exercise, and eats moderately of plain food, but is occasionally costive.

Some nine years ago the patient first noticed a severe epigastric pain, lasting over night. After that, at long intervals, he had similar pains, but of less marked severity. In the summer of 1907 he had a sudden attack of pain which had to be relieved by morphine, and since then the attacks have been somewhat more frequent. The last one was about six weeks before the present illness, and again morphine was used. In all of these attacks the paroxysm, while severe, has been of comparatively short duration and unaccompanied by jaundice.

On December 15, 1907, the patient again had severe abdominal pain during the night. He obtained relief from a small hypodermic injection of morphine, but for the next two days had more or less epigastric uneasiness and did not feel well. On December 16, when seen by me, he had some tenderness in the epigastrium, to the left and below the ensiform cartilage. On the following day the pain increased, but no morphine was required. Lavage of the stomach with about a quart of warm water appeared to give him relief. On the next day, December 18, 1907, the patient went to business, but still felt uncomfortable. About seven o'clock on the evening of this day he was seized with severe, agonizing pain in the epigastrium, and soon after this vomited.

Physical examination at this time showed the patient to be suffering severe pain, which was localized in the epigastrium to the left of the median line. A hypodermic injection of one-fourth grain of morphine, followed soon after by half that amount, gave only partial relief. The temperature was 95°, the pulse ranged from 80 to 90 per minute. The patient's skin had a sallow hue, he was perspiring freely, and his extremities were cold. He complained of slight epigastric tenderness and some nausea, and at times regurgitated a small amount of greenish fluid. Olive oil and calomel given during the night and next morning were also vomited. In the next two days the patient developed slight jaundice, which disappeared at the end of forty-eight hours. His bowels did not move until the second day. Elevation of temperature up to 100.2° was at times noted, and the pulse became rapid, weak, and irregular. The vomiting became less, but did not cease, and in the intervals the patient was troubled by persistant belching, which caused him great pain. Epigastric distention developed about December 20, and gradually became more marked. Associated with this was some slight rigidity of the left rectus muscle with epigastric tenderness. The gastric tympany extended to the navel, and the heart apex was pushed upward an interspace. About four days after the acute onset there was noted limited expansion of the left chest, some tenderness in the left loin, and a suggestion of a friction sound in the left axilla. The bowels were moved by enemas, but flatulence continued to distress the patient. The patient's general condition was one of marked toxemia, greatest at about December 21. His pulse was rapid and weak, the respirations were from 34 to 50 per minute, and the temperature irregularly febrile, but never exceeding

101°. The hemoglobin was low, at one time 56 per cent., while there was a continued and increasing leukocystosis, reaching a maximum of 23,400 on December 25. At no time, however, was there an excess of polymorphonuclear leukocytes.

The patient gradually improved as to his general condition. He was seen in consultation by Dr. John B. Deaver and Dr. John H. Musser, of Philadelphia, and on December 26, by Dr. Reginald Fitz, of Boston. At this time there was noted a deep-seated, not tender mass in the epigastric and upper umbilical regions, which was apparently continued into the left loin. There was marked tenderness in the left flank. The epigastrium was slightly distended, but there was no rigidity of the recti muscles. The edge of the spleen was palpable and there was an extended area of dulness in the left lower axillary region. The hepatic dulness extended from nipple to navel.

Up to this time there had been no laboratory findings of importance, except the leukocyte count at various times. The urine, at first scanty and high colored, later became more free. It showed albumin and a few casts, but no sugar. The Cammidge test was performed twice, once with positive and once with negative result.

The diagnosis of acute pancreatitis was first made December 21, and on December 26 all the signs pointed to an accompanying omental bursitis, without, however, an accompanying peritonitis. Operation was considered as being indicated, the only cause of delay being the hope of still further improvement in the patient's condition. This occurred in the next few days, and justified our postponement of operation.

The treatment medically up to the time of operation was comparatively simple. The patient was kept on very light liquid diet, and, as occasion required, was given small doses of strychnine. His bowels were kept open by enemas at first, but later these were not needed. At the time of greatest depression continuous saline enteroclysis by the Murphy method was given, and seemed to cause marked improvement both in the patient's general condition and in the kidney function.

On December 27, 1908, the patient was removed to the German hospital. On December 28, 1908, he was operated upon by Dr. John B. Deaver, under ether narcosis. The pancreatic collection was approached by the extraperitoneal route through the left loin, the incision being exactly as for a kidney operation. When the location of the pancreas was reached, thick dark necrotic material was evacuated. There was some fat necrosis of the fatty tissues along the line of entrance to the omental bursa. No attempt was made to do anything but drain the peripancreatic space and the omental bursa. This was done by means of two rubber tubes of large caliber; several gauze tampons were also introduced.

The cultures from the necrotic material removed at operation were negative, as were also those from a slight amount of clear fluid aspirated into a hypodermic needle at operation, which seemed to come from just beneath the muscles and from a point above the necrotic and purulent material.

The patient left the operating room in good condition. For a week after the operation his pulse continued rapid, his respirations were above the normal, and the temperature showed marked fluctuations. It was often subnormal in the morning, and reached a maximum in the evening of 103.4°. The patient complained at times of chilly sensations and nausea.

On December 31 the leukocytes rose to 31,800, but with only 76.5 per cent. of polymorphonuclears and 15.5 per cent. of transitional cells. The lymphocytes, large and small, were but 6.5 per cent. On January 9 the left chest was aspirated because of the still persisting dulness there, but no fluid was found. On January 8 a large slough was removed from the wound 4 x 2 x 2 cm. in size; microscopic section showed it to be necrotic pancreas. The wound after this seemed to discharge less, but the discharge again became very free. Twelve days later a portion of gangrenous pancreas (confirmed microscopically) 6 x 3½ x 3 cm. was removed, and on the following day, perhaps because of trauma by the instruments, there was a profuse hemorrhage from the wound. The wound was tightly packed, and after that improved steadily, although still existing in the form of a small discharging sinus at the time of the patient's discharge from the hospital on March 12. The discharge from the wound was always very irritating to the skin, and analysis showed it to consist of pancreatic secretion and pus cells. Trypsin was present in it.

After the operation the patient's temperature was irregular for a time, but gradually dropped to the normal level. The treatment was such as would be given after any grave operation. Some difficulty was experienced in regulating his diet at first, but no digestants except a little pepsin were given. The urine during his stay in the hospital was at no time scanty, and showed no sugar, but always contained a few casts and a trace of albumin.

At the present time the patient is in perfect health. The sinus has permanently healed, after several temporary closures just after he left the hospital. He has had no glycosuria, has gained flesh, and digests all foods, although he has had several slight attacks of indigestion.

An examination of his metabolism by Dr. D. L. Edsall, of Philadelphia, shows it to be practically normal and very satisfactory, considering his recent disturbance. While taking a diet liberally supplied with fat, an average of 103.5 grams a day, he absorbed 93.8 per cent., good even for a normal person. He absorbed 90.1 per cent. of nitrogen, a little below the normal, and the stools contained 1.8 grams a day, which also showed rather poor absorption. He excreted an average of 12.3 grams of nitrogen in the urine, hence with the 1.8 grams in the feces he lost 14.1 grams daily while taking 17.9 grams. Hence he retained a daily average of 3.8 grams, which he was evidently using in building tissue.

A case such as this furnishes many points of interest from a purely surgical point of view, but to the practitioner or clinician the etiology and diagnosis are of paramount importance. I shall, therefore, scarcely refer to the surgical aspects of the case, and confine my remarks to the clinical features of this particular case.

As to the etiology we must be somewhat uncertain. The patient was not of the obese and alcoholic type usually said to be associated with acute pancreatitis, although a review of the later literature shows this to be less often so than was formerly supposed. The repeated attacks of transient colicky pain, with slight evidences of indigestion and constipation at times present, render a diagnosis of biliary calculus probable, even in the absence of jaundice at any time. The attacks of pain might be considered as being due to pancreatic lithiasis, but in the absence of marked signs of disturbance in the pancreatic function this is untenable. Indeed, this diagnosis has so rarely been correctly made that we may well leave it entirely out of consideration. It is possible that cholelithiasis was the underlying cause of the acute pancreatic lesion. Its direct causation is open to question. It is undoubtedly an "acute" case, yet at operation there was no evidence that a large amount of blood had been lost, although some degenerated blood pigment, etc., was present. It seems likely, in view of the patient's previous good health, and of a few days of indefinite illness before the actual onset of ultra acute manifestations, that pancreatic inflammation preceded the hemorrhage. The two factors mentioned are the only ones upon which we can base such a supposition, because clinically such a distinction at the time of onset is, of course, impossible. On this assumption, then, the course was that of some biliary infection producing a mild inflammatory condition of the pancreas, and this in turn producing a hemorrhage. Following the hemorrhage a typical gangrenous pancreatitis occurred, such as would be expected after interference with the blood supply of a large portion of the organ. A patient in whom this is the sequence of events would seem to stand a somewhat better chance of recovery than one in whom the hemorrhage is primary, due to a diseased bloodvessel wall. In such case we have to deal not only with the grave local lesion, but also with the general arteriosclerosis, of which the pancreatic apoplexy is only a terminal manifestation.

The further course of the case as a gangrenous pancreatitis is to be distinguished from those in which a localized pancreatic infection causes a purulent condition of parts of the organ and its surrounding tissues. The former affection is undoubtedly the more grave.

The diagnosis in any case of acute pancreatitis is usually not easy. In this instance the rule holds good. At various stages of the disease during the first few days a number of conditions were simulated, at least to such a degree that a definite diagnosis was impossible. Before the acute paroxysmal onset of the graver symptoms the case presented no evidence of being anything more than perhaps an atypical form of gastritis or gastroduodenitis. The patient seemed slightly more ill than he should be under those conditions, but nothing definite supervened. At the time of the acute attack of pain, that is, the actual beginning of the gangrenous pancreatitis, there was nothing pathognomonic, yet the symptoms were suggestive. At that time they were: agonizing epigastric pain, subnormal temperature, slow full pulse, and absence of a localized point of tenderness or local abdominal signs.

The pain might be taken to resemble that of either a perforating peritonitis of the upper abdomen or an attack of gallstone colic. It was referred to the epigastrium and at times to the left thereof, but not with any great degree of definiteness. As against possible gallstone colic we have the absence of any radiation to the shoulders, back, etc. But it may safely be stated that at its very onset it was impossible to differentiate this pain from either of those mentioned. The subnormal temperature would occur in any severe sudden abdominal trauma, and depends upon the associated shock. Of more importance is the pulse. This in the attack was slow, regular, and of good volume. The association of a good slow pulse with subnormal temperature and shock is infrequent. Especially does it serve to eliminate from the diagnosis a perforative peritonitis, for in this the pulse practically always is rapid and often weak.

The association of slow pulse with acute pancreatitis has been dwelt upon by the later German investigators, notably Noetzel and Doberaner, both of whom have noted but have not attempted to explain the condition. Mayo Robson does not speak of it, however. John B. Deaver states that in his experience the presence of a slow pulse at the very onset of the attack is common. This must, however, not be confused with the pulse condition some hours later. In practically every instance of a true acute hemorrhagic or gangrenous pancreatitis the pulse in a very short time becomes rapid, weak, and often irregular, as in the present instance. Cyanosis, often included in the syndrome of an acute pancreatitis, was absent in this instance, as were also any definite localizing signs in the abdomen at the onset of the attack.

The diagnosis then at the onset was impossible, but within twenty-four hours certain added features tended to make a definite diagnosis possible. Obstinate constipation supervened, which could not be overcome by ordinary means. Vomiting, which had occurred once before the acute attack of pain, now took place several times in the twenty-four hours. Both of these conditions are practically always present in acute pancreatitis. More important, however, as a subjective sign was the obstinate belching. Probably due to a diaphragmatic inflammatory involvement from the inflamed retroperitoneal space, it has been noted almost without fail in every case of acute pancreatitis. Not only this, but it has been to the patient a far more distressing thing than even severe vomiting, as each eructation seems to cause great pain.

Slight icterus came on within twenty-four hours, and remained forty-eight hours. This also would point to a pancreatic or biliary condition as opposed to a lesion of one of the upper abdominal viscera. In addition to these general symptoms occurring within the first forty-eight hours, certain other local signs, together with the change in the patient's general condition, tended to make a diagnosis of pancreatic trouble stand out alone as by far the most probable.

The general condition of the patient was one of profound toxemia rather than one of infection. With a rising leukocyte count and some fever, there were no marked exacerbations in the fever, chills, etc. At the same time the depression was so profound that there could be no mistake as to the toxic condition. The differential leukocyte count also showed a persistently low percentage of polynuclears, another point in favor of a toxic agent not purely bacterial in origin. And, indeed, recent investigations tend to show that in these cases there is a specific form of trypsin poisoning, which accounts for the constitutional condition that is so grave a feature of the disease. The local symptoms as described in the history of the case indicate, when considered in sequence, the gradual formation of an exudate deep in the upper abdomen and gravitating to the left loin.

Taken collectively, and regarded in the view of subsequent occurrences, the symptom syndrome in this case is fairly typical of acute pancreatitis. In the differential diagnosis of the case, however, we had to deal at the onset with a very acute condition, in which it was imperative to decide whether or not surgical interference was called for, and each day changed the aspect of affairs.

The differential diagnosis of acute pancreatitis under any circumstances is one of considerable difficulty. Cases have been reported in which intestinal obstruction, acute pelvic disease, acute appendicitis, etc., were simulated to a greater or less degree. I shall not attempt to enter into the general aspects of the matter, but merely to discuss it as applying to this partiticular instance. At the beginning of the illness in this case, or rather at the onset of the ultra-acute symptoms, three possibilities were to be considered. The pain was epigastric, everything pointed to an upper abdominal lesion. Therefore, acute pancreatitis, biliary colic, and the actual or impending perforation of a gastric or duodenal ulcer presented themselves. The pain resembled closely that of biliary colic, and with the history of a previous attack of pain, a preceding digestive disturbance and the patient's sallow appearance made this the first thought. Against it we had the absence of any palpable condition about the gall-bladder and of any tenderness in this region or over Mayo Robson's point. The shock with slow pulse would have been a possibility in this condition also. The subsequent course of the illness soon showed a purely biliary condition to be out of the question. The toxemia and depression, beginning epigastric swelling, tympany, and tenderness, especially to the left of the median line, proved that we had to deal with a condition more grave than simple biliary colic, even one associated with marked inflammation of the bile passages. Nothing at any time pointed to a perforative lesion of the gall-bladder or ducts. Perforated gastric or duodenal ulcer would give the pain and shock. Yet in this we should have a rapidly spreading peritonitis of the greater cavity, with its typical symptoms, with rapid running pulse, etc., unless the perforation were partly walled off or had taken place upon the posterior wall of the stomach. This is unlikely, and in any case the symptoms would more probably have been those of a septic purulent condition in the greater or lesser peritoneal cavity. The possibility was borne in mind, however, until the toxemia with belching and icterus and the localizing signs deep in the left side left no doubt as to the true condition.

A word or two as to the laboratory findings may not be out of place. They were carefully considered, but, as in most cases they should be, they were counted entirely secondary to the clinical signs. The persistently high leukocyte count, with low polynuclear percentage, pointed to an intoxication rather than a pus infection. The comparatively high count, also, pointed to better powers of resistance than a low one would have done. The absence of glycosuria, except in one doubtful test, did not weigh against the diagnosis of acute pancreatitis, for, as Körte and others have pointed out, glycosuria is a rare accompaniment of the acute pancreatic lesions. The Cammidge test was, as stated, once positive and once negative, before operation. Until it is further developed, this must still be considered more as an interesting test than an important one, at least in the acute forms of pancreatic disease.

The treatment of acute pancreatitis is, of course, surgical in all instances. To the medical man such a case as this presents but one problem, surgically speaking—that is, when to advise operation. Recent German operators who have had opportunity of seeing a number of these cases advise early operation, to avoid the toxemia, to establish drainage, etc. Doutbless this may be the correct course to pursue in many instances, yet we must be guided by the condition present. In the present case, I have no doubt that immediate operation, say within forty-eight hours, when the depression and toxemia were at a maximum, would have resulted fatally, and that by giving the patient a chance to react therefrom we gave him his one chance of recovery.

In conclusion, I wish to thank Dr. John B. Deaver and Dr. Reginald H. Fitz, of Boston, for their interest, and the use of their notes to supplement my own.

THE TYPHOID CUTANEOUS REACTION.

By Cleaveland Floyd, M.D.,
and
Williston W. Barker, M.D.,
of Boston.

In any disease, such as typhoid fever, in which the type of infection is that of a septicemia, every portion of the body is affected. This is true not only of tissue directly invaded by Bacillus typhosus, but on account of its diffusible toxins, of all the cells of the body. The dissemination of the endotoxins of the organism, through its destruction in the course of the disease, makes this possible, and when large numbers of bacilli are broken down by the action of bactericidal substances, the tissue cells become thoroughly sensitized to the poison. The rapidity of this sensitization is often marked, but it is frequently of short duration. This is accounted for partly by the relatively short period of the infection and possibly by inherent properties of the toxin itself. The union of the toxic molecule of the typhoid bacillus with the cell proteid is apparently unstable and easily broken up. In tuberculosis the converse is true. Infection is generally of long duration, and therefore the continued action of the tubercle toxin on tissue is much more lasting. Furthermore, its union with the cellular elements of the body is much closer and more stable. The old inactive lesions of tuberculosis respond to the stimulation of tuberculin for years after activity has apparently ceased. The addition of tuberculin to the conjunctiva or skin liberates locally toxic bodies, and by the unity with previously formed antibodies a reaction is produced. The reactive powers of the body to the toxin of tubercle slowly decrease with the subsidence of the lesion, but reactivity is quickly renewed when antibodies have previously been formed by the inoculation of tuberculin. In such instances the response to this stimulation is often delayed for several hours over the usual time required for a reaction.

In typhoid fever in which the infection is of relatively short duration, except occasionally in the gall-bladder, the result is different. In a previous paper it was shown that cellular sensitiveness as shown